

Committee Meeting: Validation of diffusion MRI with synchrotron x-ray micro-CT data

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Outline

- ▶ Background
 - ▶ Diffusion MRI
 - ▶ Reconstruction and validation
 - ▶ Tractography and validation
 - ▶ Synchrotron μ CT
- ▶ Potential aims
 - ▶ Aim 1: μ CT acquisition and data processing optimization
 - ▶ Aim 2: Validation of MRI ODFs with μ CT data using structure tensor analysis
 - ▶ Aim 3: Validation of MRI tractography algorithms using μ CT ODFs
- ▶ Timeline

Diffusion MRI

- ▶ Non-invasively estimates the bulk orientation-dependent diffusion within a voxel
- ▶ Data reconstructed into an orientation distribution function (ODF)
 - ▶ 3D profile of diffusion anisotropy
- ▶ It is assumed that this ODF carries information about underlying tissue microstructure

Diffusion MRI: Reconstruction methods

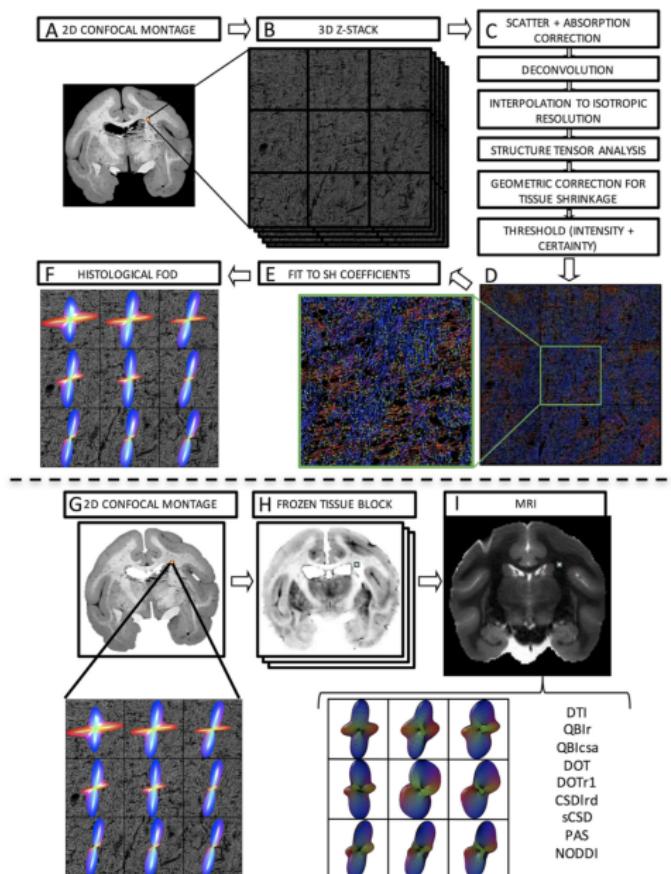


<https://www.slideshare.net/NFBI/bram-plate1>

Diffusion MRI: Previous reconstruction validation

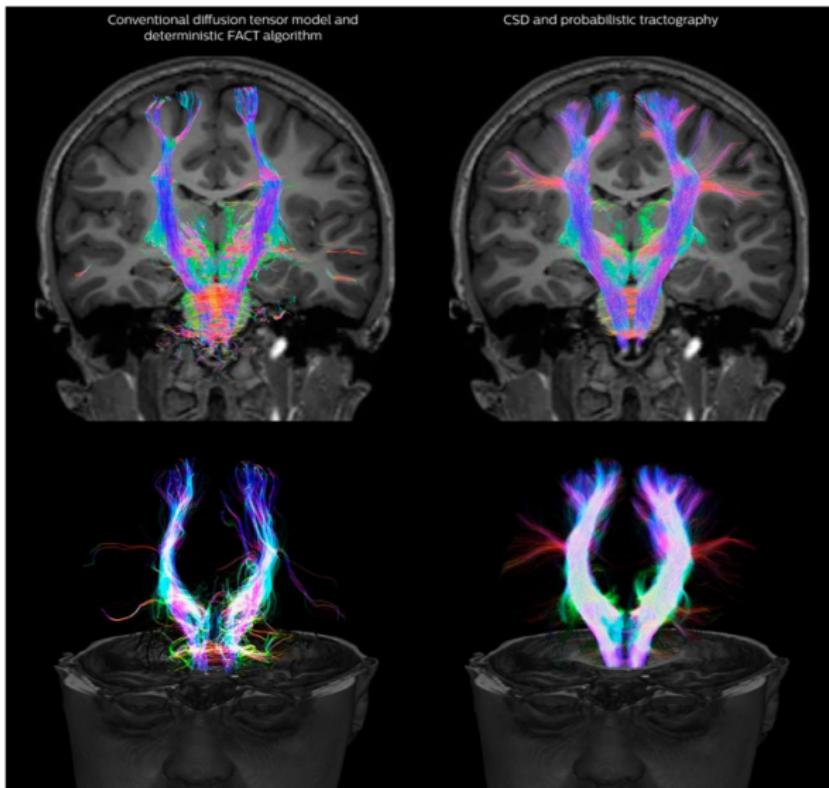
- ▶ Past groups have validated these ODF reconstructions using an image processing technique called “structure tensor analysis”
 - ▶ Uses image gradients to estimate the direction of smallest intensity variation at each voxel[1].
 - ▶ Bin these directions into a ground truth ODF
- ▶ Most groups have used 2D histology images as ground truth[2–5]
 - ▶ Others have used polarized light imaging[6, 7], and 3D confocal stacks[8–10]
- ▶ **All previous validation datasets require physical sectioning of the sample and do not have isotropic resolution in 3D.**
 - ▶ This introduces a number of additional processing steps and sources of error in the validation pipeline.

Diffusion MRI: Previous reconstruction validation



Schilling 2018[9]

Diffusion MRI: Tractography

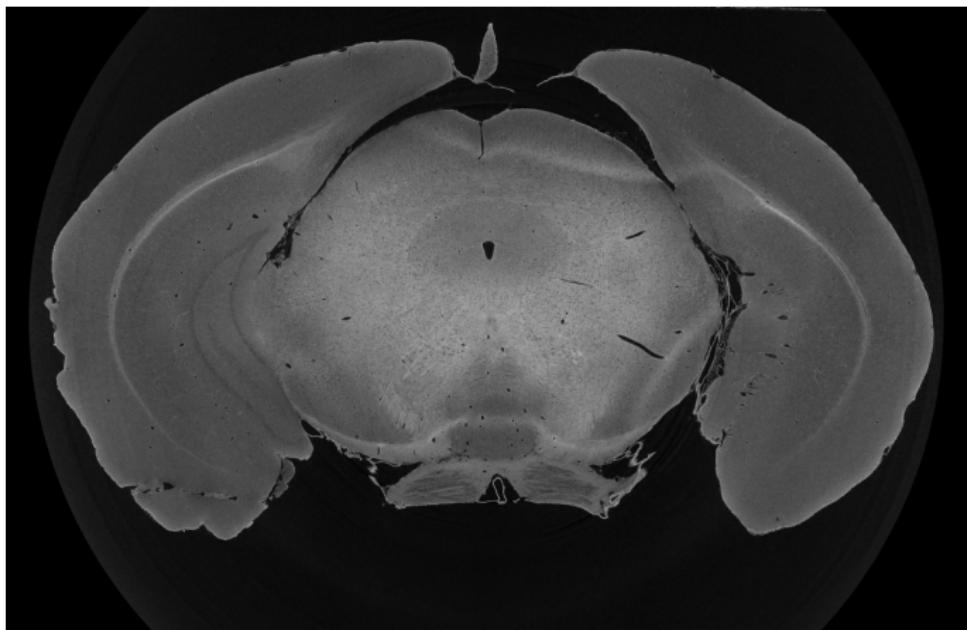


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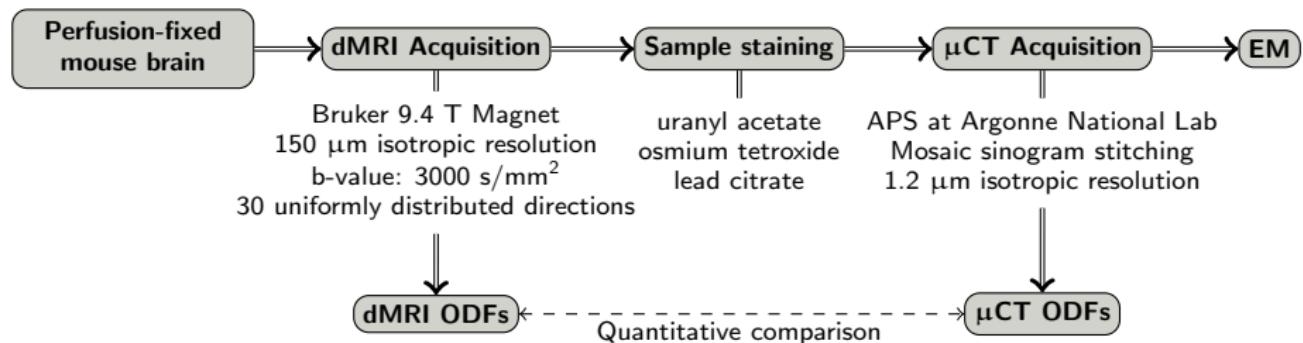
Diffusion MRI: Previous tractography validation

- ▶ Some groups have used synthetic data[11]
- ▶ Most groups have injected neural tract tracers, formed a 3D histological volume and compared the fibers to tractography results using the injection sites as seeds.[12–17]
 - ▶ Non-isotropic resolution, requires physical sectioning
 - ▶ Limited to the number of tracer injection sites
- ▶ General result is a dramatic sensitivity/specificity tradeoff
- ▶ Again, μ CT overcomes the limitations of histology as a validation dataset, and potentially allows for validation over the entire connectome.

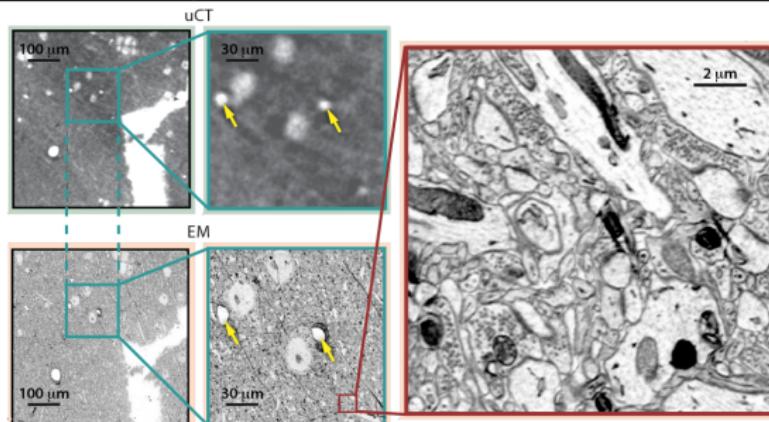
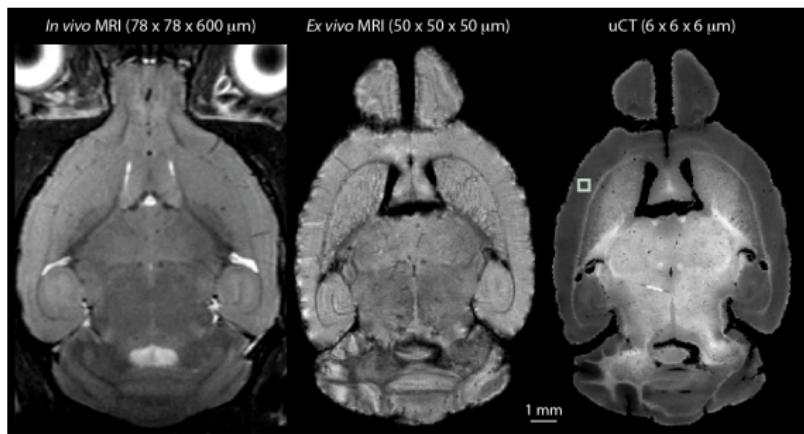
Synchrotron μ CT



Data acquisition



Data acquisition



Potential Aims

The general scope of this project will be to develop and optimize a pipeline to use synchrotron x-ray μ CT data to validate, characterize and compare diffusion MRI reconstruction and tractography algorithms.

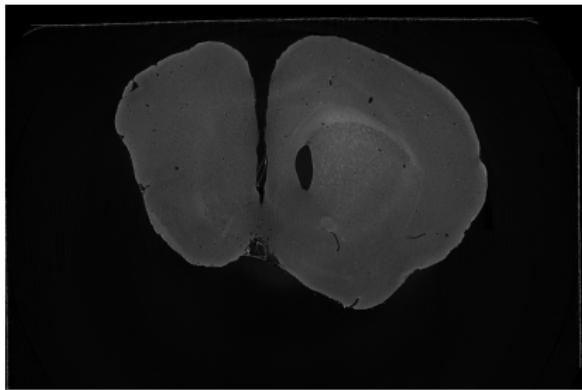
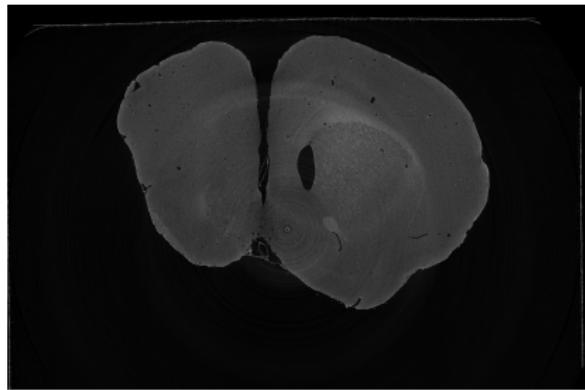
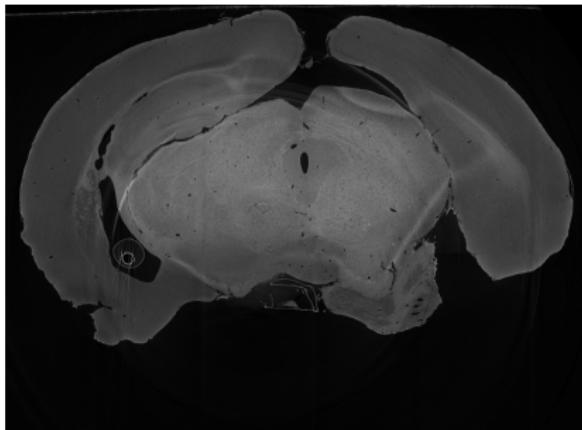
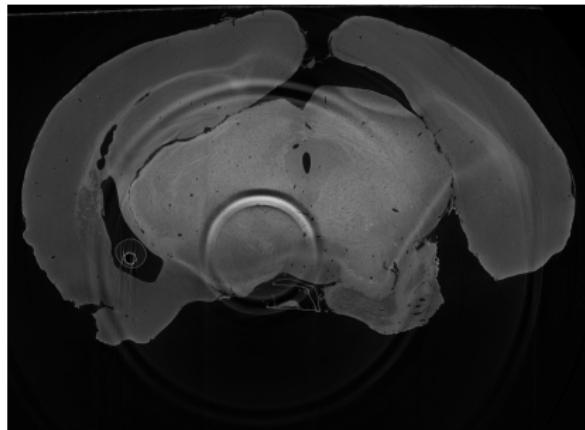
Potential Aims:

1. Optimize μ CT data acquisition, pre-processing
2. Use 3D structure tensor analysis to estimate ground truth ODFs from μ CT data and perform quantitative comparisons with ODFs from MRI
3. Use ODFs and segmented white matter tracts from the μ CT data to evaluate MRI tractography algorithms

Aim 1: μ CT data optimization

- ▶ Specifics to be determined
- ▶ Data acquisition ideas:
 - ▶ Characterize new detector hardware that is arriving soon
 - ▶ Accurately model and optimize acquisition to exploit x-ray phase contrast
 - ▶ Theoretical work on choosing beam energy to optimize CNR for metal stains
- ▶ Data processing ideas:
 - ▶ Develop efficient computational pipeline to deal with massive data size
 - ▶ Full reconstruction on the order of 5-10 TB
 - ▶ Improve collaborators' current file size reduction methods
 - ▶ Addressing ring artifacts with post-processing algorithm[18]

Ring artifacts example

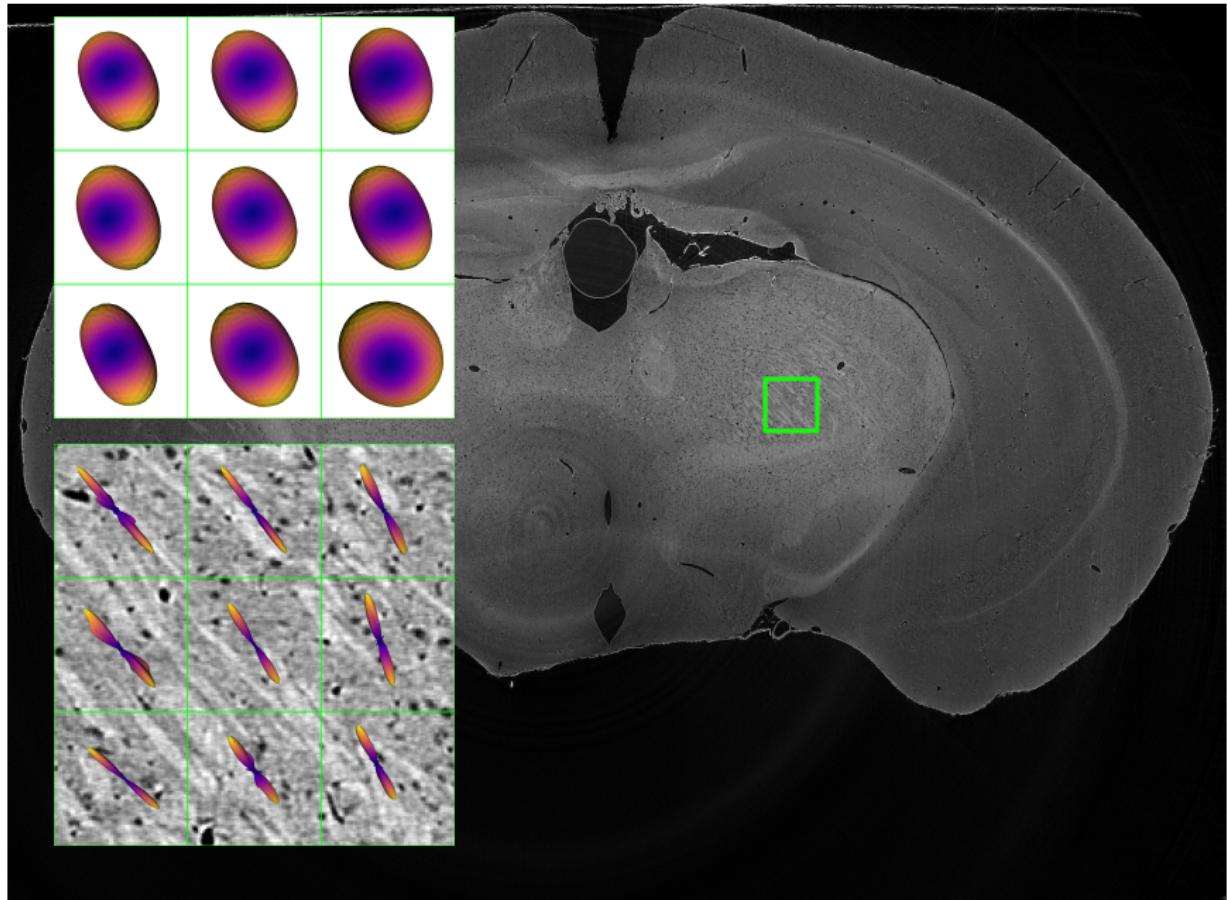


Aim 2: Validation of MRI ODFs with μ CT using structure tensor analysis

Completed work:

- ▶ μ CT ODF calculation pipeline is developed
- ▶ μ CT - MRI registration pipeline is developed and close to being implemented/validated
- ▶ Preliminary ODF comparisons look promising

Aim 2: Preliminary results



Aim 2: Registration pipeline

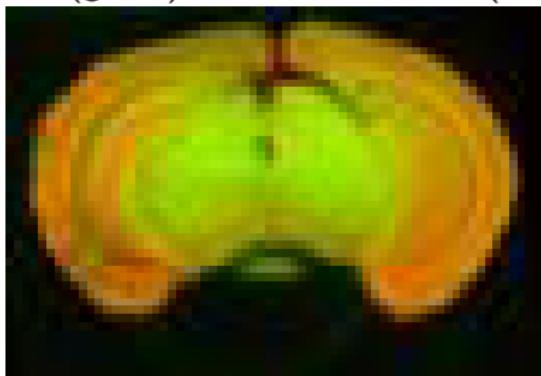
Registrations are currently being computed with ANTs software from UPenn[19, 20]

Pipeline:

1. Calculate ODFs from full-res μ CT data binned over ROI the size of a DW-MRI voxel
2. Downsample μ CT ($\sim 1.2 \mu\text{m}$) and structural MRI ($\sim 50 \mu\text{m}$) to DW-MRI resolution ($\sim 150 \mu\text{m}$)
3. Calculate linear and nonlinear diffeomorphic [21] μ CT \rightarrow structural MRI transform
4. Calculate linear structural MRI \rightarrow DW-MRI transform
5. Apply combined transforms to μ CT ODFs
6. Rotate μ CT ODFs appropriately[22–26]

Aim 2: Registration pipeline

μ CT (green) \rightarrow structural MRI (red)



structural MRI (red) \rightarrow DW-MRI (cyan)



Aim 2: Proposed work

- ▶ Replicate other groups' histology results with μ CT data
 - ▶ Use μ CT ODFs over a large number of ROI as ground truth to compare performance of a number of DW-MRI reconstruction models
 - ▶ Requires a new dataset with more directions for most HARDI algorithms
- ▶ Characterize sensitivity / uncertainty with structure tensor method
 - ▶ Large number of tunable parameters that most groups do not adequately discuss
- ▶ Potentially could get a spatial map of algorithm-specific DW-MRI reconstruction failure, characterize by tissue type, etc.

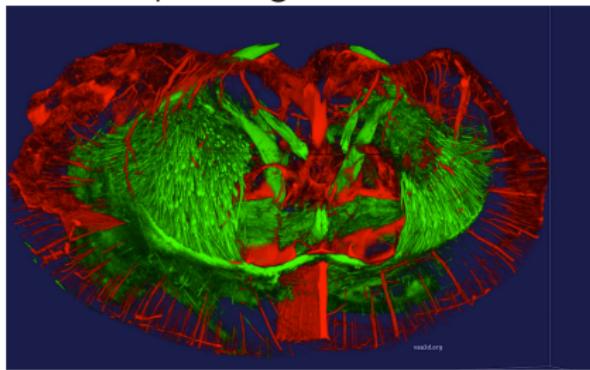
Aim 3: Tractography validation

Proposed work:

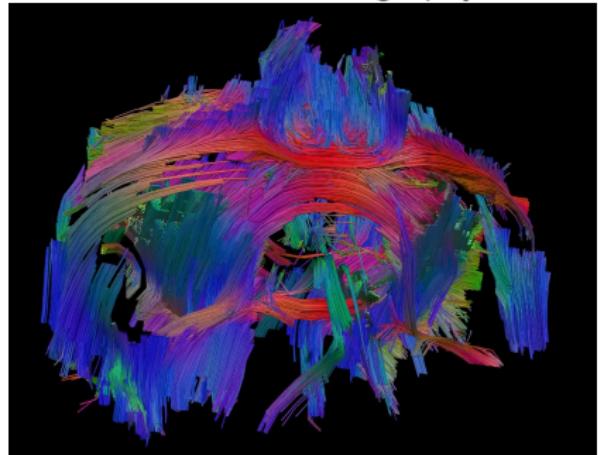
- ▶ Segment white matter tracts from μ CT data
- ▶ Compare to MRI tractography
- ▶ Compare to tractograms generated from running MRI tractography algorithms on μ CT ODFs from Aim 2
 - ▶ Eliminates registration error
 - ▶ Characterize tractography algorithm performance with many free parameters:
 - ▶ Can calculate ODFs at arbitrary “voxel size”
 - ▶ Can calculate ODFs using different models (fit to tensor instead of SH)

Segmentation vs. tractography

μ CT segmentation



DW-MRI tractography



Graduation timeline

- ▶ December 8, 2018 - submit F31 grant proposal
- ▶ Winter quarter 2019 - complete GPMP thesis proposal
- ▶ Spring 2021 - graduation

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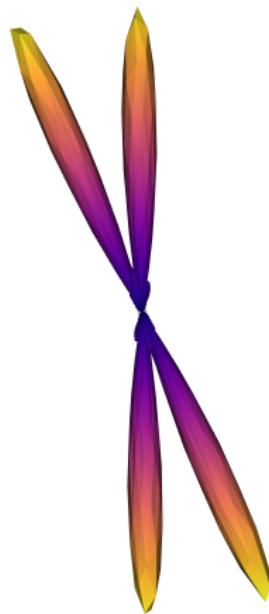
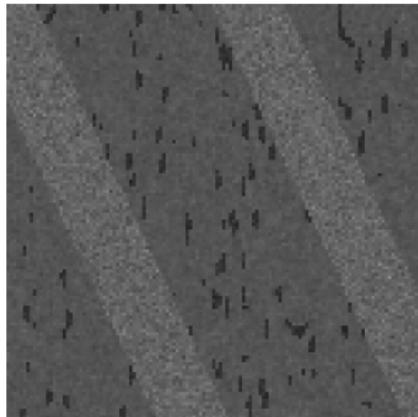
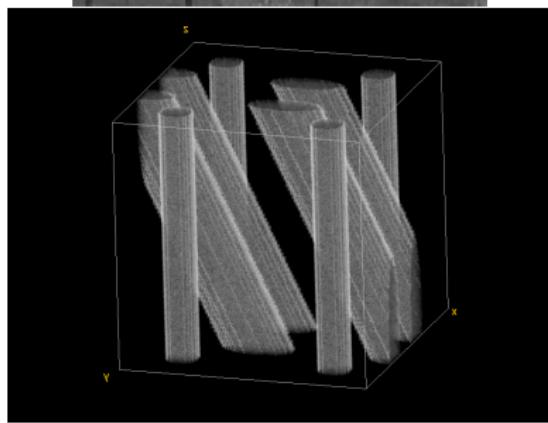
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μ CT ODFs: phantom validation



Structure tensor analysis

For a 3D intensity image $f(x, y, z)$, with gradient $\nabla f = (f_x, f_y, f_z)$:

$$\text{ST}(f)(x, y, z) = g_{\sigma_N} \circledast \begin{pmatrix} f_x^2 & f_x f_y & f_x f_z \\ f_x f_y & f_y^2 & f_y f_z \\ f_x f_z & f_y f_z & f_z^2 \end{pmatrix}$$

The eigenvector with the smallest eigenvalue is an estimate of local fiber orientation. In an ROI containing K such fiber orientation vectors, the ODF can be written in spherical coordinates:

$$\text{ODF}(\theta, \phi) = \frac{1}{K} \sum_{k=1}^K \delta(\theta - \theta_k) \delta(\phi - \phi_k)$$

The ODF can be expanded on the real spherical harmonics, $Y_l^m(\theta, \phi)$, up to degree L_{\max} :

$$\hat{\text{ODF}}(\theta, \phi) = \sum_{l=0}^{L_{\max}} \sum_{m=-l}^l c_{lm} Y_l^m(\theta, \phi)$$